REMARKS

Applicants request reconsideration of the above-identified application in view of the foregoing amendments and the following remarks.

Claims 12 and 38-40 are pending in the present application. Applicants have canceled claims 38 and 40 without prejudice. Applicants have amended claims 12 and 39 and have added claims 41-42 to more particularly point out and distinctly claim the invention. Added claims 41-42 are supported in the specification. See, e.g., page 8, lines 1-7 and Table 1, page 40. These amendments and additions do not constitute new matter.

I. Oath

The previously filed substitute Declaration and Power of Attorney executed by inventors Karpusas and Thomas were signed and dated and identified the application by application number and filing date (copies enclosed at Tab E). A substitute Declaration and Power of Attorney, signed and dated by inventor Singh, is enclosed herewith. Hence, the objection to a defective declaration is overcome.

II. Abstract

The Abstract stands objected for not being directed to the subject matter of the pending claims. Applicants have enclosed herewith a Substitute Abstract at Tab B. The Substitute Abstract is directed to the subject matter of the pending claims. The Substitute Abstract does not add new matter. See, e.g., claims 12, 39 and 41-42. See also page 8, lines 1-7, page 38, lines 17-18, page 19, line 26 to page 21, line 33, page 1, lines 3-4 and Table 1, page 40. Hence, the objection to the Abstract is overcome.

III. Claim Rejections under 35 U.S.C. § 112, 1st Paragraph

Claims 12 and 38-40 stand rejected under 35 U.S.C. § 112, first paragraph, for purported lack of enablement. Specifically, the Examiner maintains that applicants only enable a computer readable storage medium comprising data capable of displaying the three dimensional structure of human CD40L residues 116-261, and a computer comprising said medium. Applicants traverse.

Applicants have canceled claims 38 and 40 without prejudice. The rejection of those two claims is therefore moot.

The Examiner asserts that the specification, while exemplifying a method for crystallizing and

obtaining structure coordinates for residues 116-261 of a human CD40L, does not teach a person skilled in the art how to solve crystal structures of mutant or homologous CD40L molecules. The Examiner also asserts that, in claims 12 and 38-40, recitation of "a crystal of a molecule or molecular complex comprising a fragment" or the recitation of "fragment having a binding site for CD40" encompasses a fragment greater than CD40L amino acid residues 116-261 and that fragment is not enabled by the specification.

Applicants maintain that the specification discloses a method for crystallizing and obtaining structure coordinates of CD40 ligand proteins and provides an example thereof. See specification, pages 33-40. Furthermore, the specification teaches a person skilled in the art as of the effective filing date of this application how to obtain, for example, by molecular replacement methods, the structures of crystal forms of CD40L or CD40L mutants, other than that exemplified, without undue experimentation. See, e.g., the specification at page 14, lines 8-33 and page 24, line 22 to page 25, line 4. A person skilled in the art as of the effective filing date of this application would also appreciate that the extracellular domain of CD40L, as well as full-length CD40L, binds to CD40. Therefore, the

structure of the binding site for CD40 on either molecule would be similar, as would any variants or mutants of CD40L comprising the binding site of CD40L for CD40.

Thus, the structure coordinates of the extracellular domain of CD40L enables a person skilled in the art to obtain the structure of full-length CD40L, variants and mutants of CD40L, by molecular replacement methods.

Accordingly, claims 12 and 39 are enabled as to their present scope and thus satisfy 35 U.S.C. § 112, first paragraph. The same is true for added claims 41-42.

IV. Claim Rejections under 35 U.S.C. § 112, 2nd Paragraph

Claims 12 and 38-40 stand rejected under 35 U.S.C. § 112, second paragraph, as being "indefinite" for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Applicants traverse.

The Examiner asserts that "[r]ecitation of a Table . . . in the specification renders the claims indefinite as it is unclear what limitations are intended to be incorporate in the claims." Specifically, the Examiner contends that it is unclear whether all the coordinates in Table 1 are meant to be included, or only the coordinates of CD40L corresponding to Lys143, Arg203,

Arg207 and Tyr145 (which correspond to residues 28, 88, 92 and 30 of SEQ ID NO: 3 respectively). The Examiner also asserts that Table 1 includes multiple coordinates for each amino acid.

Table 1 displays the structure coordinates of human CD40L amino acids 116 to 261, as determined by X-ray crystallography. There is only one set of coordinates. The multiple references to a single amino acid in Table 1 are to different atoms of that amino acid.

Amended claims 12 and 39 are directed to data that is capable of displaying a 3-D representation of a crystal of a molecule or molecular complex comprising a CD40 binding site on CD40L.* That binding site structure is defined by at least the structure coordinates of CD40L residues Lys143, Arg203, Arg207 and Tyr145. The structure coordinates of these four residues alone require 61 lines from Table 1. See Table 1, page 40/5, 40/15 and 40/16.

Added claims 41-42 are directed to data comprising at least a portion of the structure coordinates of the CD40 ligand amino acids 116 to 261 according to Table 1. Table 1 is 25 pages long.

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* These amendments do not encompass new matter. See the specification at page 38, lines 17-18, page 19, line 26 to page 21, line 33, page 1, lines 3-4 and Table 1, page 40.

Reference to Table 1 is proper "where there is no practical way to define the invention in words where it is more concise to incorporate by reference than duplicating a. . . table into the claim." See MPEP 7th Ed., 2173.05(s) (internal citation omitted). In the present case, there is no practical way to list the required structure coordinates in the claims.

Applicants have canceled claims 38 and 40 without prejudice. The rejection of those two claims is therefore moot.

The Examiner also asserts that reference to CD40L amino acids Lys143, Arg203, Arg207 and Tyr145 and CD40L amino acids 116 to 261 is indefinite. Applicants have amended claims 12 and 38-40 according to the Examiner's suggestion, so that references for these amino acids are also made with respect to the corresponding amino acid residues in SEQ ID NO: 3. These amendments do not encompass new matter. SEQ ID NO: 3 of the Sequence Listing* is the sequence of the human CD40L (amino acids 116-261). CD40L amino acids 116 to 261 correspond to residues 1 to 146 of SEQ ID NO: 3. Lys143, Arg203, Arg207 and Tyr145 correspond to residues 28, 88, 92 and 30 of SEQ ID NO: 3, respectively.

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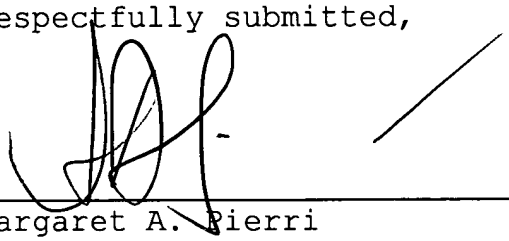
* A Sequence Listing including the sequences of Figure 5 was filed on December 26, 2000.

Applicants have also amended the specification at page 10 so that the description of Figure 5 reflects the sequences of the Sequence Listing. That amendment does not encompass new matter. The Sequence Listing filed on December 26, 2000 includes the sequences of Figure 5.

For all of the foregoing reasons, amended claims 12 and 39 and added claims 41-42 satisfy 35 U.S.C. § 112, second paragraph.

Applicants request that the Examiner enter the foregoing amendments, consider the foregoing remarks and pass this application to issue.

Respectfully submitted,



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August 10, 2001
Lillian Garcia

Signature of Person Signing

Appendix to Specification Amendments

Figure 5 is a sequence alignment of the TNF-like domains of TNFα (SEQ ID NO: 1), LTα (SEQ ID NO: 2) and CD40L (SEQ ID NO: 3) based on structural considerations.

ABSTRACT

The present invention relates to crystals of fragments of CD40 ligand, specifically, a soluble fragment of CD40 ligand (116-261). The invention relates further to uses of these crystals and the coordinates thereof to design, identify, optimize or characterize chemical entities having properties of interest.

The present invention also relates to a machine readable medium comprising a machine readable storage material encoded with machine readable data, wherein said data comprises at least a portion of the structure coordinates of a fragment of CD40 ligand, and wherein said data, when read by an appropriate machine, is capable of displaying a three dimensional representation of a crystal of a molecule or a molecular complex comprising a fragment of CD40 ligand. The present invention further relates to a machine comprising said medium.

Appendix to Abstract Amendment

ABSTRACT

The present invention relates to crystals of fragments of CD40 ligand, specifically, a soluble fragment of CD40 ligand (116-261). The invention relates further to uses of these crystals and the coordinates thereof to design, identify, optimize or characterize chemical entities having properties of interest.

The present invention also relates to a machine readable medium comprising a machine readable storage material encoded with machine readable data, wherein said data comprises at least a portion of the structure coordinates of a fragment of CD40 ligand, and wherein said data, when read by an appropriate machine, is capable of displaying a three dimensional representation of a crystal of a molecule or a molecular complex comprising a fragment of CD40 ligand. The present invention further relates to a machine comprising said medium.

Appendix to Claim Amendments

12. (Twice Amended) A machine readable data storage medium comprising a data storage material encoded with machine readable data which, when read by an appropriate machine, is capable of displaying a three dimensional representation of a crystal of a molecule or molecular complex comprising [a fragment of CD40 ligand having] a binding site for CD40 comprising CD40 ligand amino acids Lys143, Arg203, Arg207 and Tyr145, which correspond to residues 28, 88, 92 and 30, respectively, of SEQ ID NO: 3, wherein said data comprises the structure coordinates of CD40 ligand amino acids Lys143, Arg203, Arg207 and Tyr145 according to Table 1.

39. (Amended) A machine comprising a machine readable data storage medium comprising a data storage material encoded with machine readable data which, when read by said machine, is capable of displaying a three dimensional representation of a crystal of a molecule or molecular complex comprising [a fragment of CD40 ligand having] a binding site for CD40 comprising CD40 ligand amino acids Lys143, Arg203, Arg207 and Tyr145, which correspond to residues 28, 88, 92 and 30, respectively, of SEQ ID NO: 3, wherein said data comprises the structure coordinates of

CD40 ligand amino acids Lys143, Arg203, Arg207 and Tyr145 according to Table 1.